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To: Dr. Meg Oeller
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From: Dr. Gareth Moore
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Sorry for leaving this till the last minute. Hope you get a chance to read it before discussing it tomorrow!

Thanks,

Gareth.

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Comments from Gareth A. Moore, DVM, MS, Dip (ABVP)
Drug and Biologics Availability Committee Chairman
American Association of Small Ruminant Practitioners on CVM/FDA's:

"PROPOSALS TO INCREASE THE AVAILABILITY OF APPROVED ANIMAL DRUGS FOR MINOR SPECIES AND MINOR USES"

As a group the American Association of Small Ruminant Practitioners are significantly affected by the on going problem of drug availability in minor and exotic species. Recent legislative action (AMDUCA and ADAA) offers the possibility of dramatic change with regard to this situation. Ongoing efforts by the CVM/FDA to potentially improve drug availability for the species we deal with are appreciated.

As to specific comments on the recent proposal:

Section I; A) This preamble seems to imply that minor species are maintained more for novelty value rather than as production species. While this may be true for species maintained in zoological parks it is most certainly not true for the various aquatic and bird species farmed for food or for sheep and goat breeds producing meat, milk and fiber. While the economic impact of the so-called major species is greater than these minor species the latter do contribute a significant amount to the national economy.

Section I; B) The concept of ELUD by veterinarians should be maintained in some form. As with the human medical community there are always going to be situations where knowledge outstrips the approval process and effective treatments will involve drug use that is not discussed on the product label. But as with the human medical community such use should always be supervised by a licensed practitioner. Since the current ELUD provisions do not allow for use of drugs except in an effort to "relieve pain and suffering in a patient" some provision must be made to approve the use of certain production enhancing pharmaceutical agents in minor species.

Section I; C) Extrapolation of data between species for the purpose of label drug approval should be a "doable" process. Perhaps limited, low cost confirmatory trials would be needed but it should work. Final clarification of the, "sheep as a minor species" rather than "major for human food safety and minor for species approval", situation must be made.

Section I; D) The move for change on the part of the CVM/FDA is appreciated.

Section III; A) See comment on Section I; C above.

Section III; B) Supplemental approvals also should be a method that works to improve minor species and minor use drug availability. NRSP-7 funded studies have produced useful information but there often seems to be a time lag or complete failure in moving from the study to an appropriate change on the product label.

Section III; C) No question, drug manufacturing for minor species and/or minor uses must meet the same guidelines as for major species use.

Section III; D) Defining non-food life stages for livestock species, for example breeding age populations, probably would not be a good idea since the possibility always exists that animals classified as such could end up being processed for human food.

Section III; E) Harmonization of international regulatory matters should occur. All the major pharmaceutical companies are international corporations and global trade in foods of

animal origin are significant. Much extralabel drug use in the past has been based on a drug sponsor's studies conducted to gain approval for a "minor" species in another country. Acceptance of such studies to allow labeling of products in this country would go a long way towards eliminating minor species /minor use problems.

Section III; F) NRSP-7 is a system that seems to work to generate useful data on drug use in minor species and minor use situations. As stated above, the problem seems to lie in moving from the NRSP-7 sponsored study to a product label with an approved use on it. A slight problem with the NRSP-7 programs has been it's legislated emphasis on research involving drugs used for disease treatment rather than disease prevention and production enhancement.

Section III; G) Clarification of the exact status of sheep, as a minor verses major/minor species, should be addressed in this area.

Section IV; A) The possibility of extralabel drug use under the supervision of a veterinarian must be maintained. Restrictions to ensure the safety of human foods must be in place but no drug approval process can meet pharmaceutical needs for all conditions in all species under all circumstances. Modifications to labeled indications should minimize the need for such extralabel use but such modifications must meet the needs of the animal industry with regard to pharmaceuticals in feed and for production enhancing drug use in certain species. Since the use of antibiotics in the major species is apparently a risk in the development of antimicrobial resistance control measures put in place to minimize that risk should be effective if applied to such use in minor species. If approvals for minor species/ minor uses are not forth coming during the first half of the sunset period this issue would have to be addressed again. It would be hoped that other provisions in this proposal would encourage drug companies to seek such approvals including those relating to production enhancing agents such as growth promotants and reproductive regulators

Section IV; B) The described methods to effect the removal of disincentives should help encourage the drug companies to seek approvals. But congressional action to allow removal of a particular drug from the market solely for lack of a FDA approval seems a bit drastic. Over the past 30 years the FDA has removed many drugs, seemingly at an increasing pace, from the American and world veterinary markets without such legislation and increased legislative power to achieve such an end seems unnecessary.

Section IV; C) NRSP-7 is a good program except for the apparent problem of moving from the development of research data to actually adding a minor species/minor use approval to a manufacturer's label. Could it do better with more money - probably yes. Could current government funding be improved if all available resources were evaluated and applied to the most effective program(s?) - certainly yes. Do we need another level of administration or a parallel agency to do this - definitively NO. Work with what you have and redirect or increase funding to whoever is doing the most effective job.

Expand and/or redefine the guidelines of the NRSP-7 program to allow its research money to be spent on production enhancement drugs (reproductive regulators and disease prevention agents - including vaccines??) not just antimicrobial treatment drugs.

Database development should be an important aspect of expanding minor species/minor use drug availability. It should also be an important aspect of maintaining the safety of such use. If practitioners seeking methods of treatment for specific conditions could be provided with current, scientifically accurate information on the use of a particular drug including human health risks, withdrawal times, etc. then the likelihood of its safe use would be much increased.

Sources of information for such a database could include:
- information from a sponsor's initial drug development (gained through FOI act action if not available any other way);
- any NRSP-7 information (gained from Public Master Files or from funded academic or industry researchers);
- FARAD database;
- USP human and veterinary drug databases;
- some tie in to international data available (again drug sponsor's files, Codex Veterinarius, WHO data, ...);
- CDC's or NVSL's databases on antimicrobial susceptibility testing, to increase awareness of potential resistance problems;
- ....

To be cost effective such a database should probably be established as a website on the world wide web. Such a website would be useful to practicing veterinarians researching effective treatments and to individuals or companies seeking potential opportunities to profit from expanded drug approvals. But if such a website is to be successful it must be managed well and kept up to date even if that involves contracting the maintenance of such a site to an outside agency with greater computer expertise.

Section IV; D) Since the pharmaceutical industry is profit driven some type of financial incentive to encourage seeking additional approvals for their products is probably needed. But in getting a product approved for major species use such companies must have determined that that market alone was sufficient to make a profit otherwise product development would have been halted. Since additional sales of a drug through a change in label indications for minor species/uses presumably increases profits then the company should collaborate by providing at least some research funding (money or facilities) to gain the information required for such additions. Making such costs for minor species/uses development tax deductible should be a reasonable incentive.
However since government money, funding from NRSP-7 or CVM/FDA assistance for example, is probably going to be used in gaining additional label indications then any additional profit potential for the sponsoring company should be examined carefully. The granting of expanded exclusivity (either use or time based) may be too costly an incentive. As is noted in the proposal such a step could effectively increase the cost of a drug to the veterinarian and producer thereby potentially limiting its usefulness.

Section IV; E) Tie such data sharing requirements into the development of the minor species/uses database. The company should stand behind any labeled uses but how to protect the animal owner from loss or the prescribing veterinarian from liability would remain a problem. (I suppose there's no possibility for reestablishing the concept of informed risk in the current lawsuit-driven American society.)

Section IV; F) The existence of a minor species/uses database and the continued, well regulated policy of extra label drug use should make the development of a minor use category or orphan veterinary drug classification unnecessary.

Section IV; G) From the sheep and goat practitioner's standpoint the idea that a drug which achieves special non-food, minor species approval is then excluded from use in food producing minor species under any circumstances is worrying. That may not be the way the CVM/FDA intends that this proposal be applied but it could be the way it is interpreted.

Section IV; H) Any such review would require CVM/FDA oversight but why limit the potential for such expert review to non-food minor species.

Section IV; I) As commented above, data generated internationally to gain drug approvals related to minor species/uses situations (as defined by the CVM/FDA) should be eligible for review by the CVM/FDA with the potential to add portions of the foreign approved label to the product marketed in the United States. Any mechanism, suitable reviewed, that simplifies such label changes should be considered.

Sincerely,

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